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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,364	07/09/2002	Alan Edward Richardson	37-02	7785

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,364	RICHARDSON ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 37-51* is/are pending in the application.

4a) Of the above claim(s) *5,11-25,40 and 44-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-10, 26-33, 37-39, 41-43, and 50-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/7/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-33, and 37-51 are pending.

2. Applicant's election with traverse of Group I, claims 1-10 and 26-33, including SEQ ID NO:4 in the reply filed on 9/29/2004 is acknowledged. The traversal is on the ground(s) that Applicants contend the amended claims are free of the prior art and request reconsideration of the restriction requirement in view of the amendments made herein (paragraph bridging pages 11-12 and page 12, 1st full paragraph).

This is not found persuasive because the amendment to recite the presence of phytate in the growing medium does not distinguish the claims over the prior art. As admitted by Applicants, phytate is ubiquitous in agricultural soils, due to the previous applications of phytate-containing fertilizers, the presence of animal manure, derivation from organic matter such as senescent plant material, etc (See page 5 of the specification, lines 10-17; page 6, lines 4-5; page 8, lines 30-31; and page 9, lines 1-4). Thus claim 1 and dependents read on a method for cultivating a transgenic plant encoding phytase in an agricultural field, which method is taught by the prior art including Austin-Phillips et al cited previously. Furthermore, the claims are in fact subjected to additional art rejections, as stated below.

The requirement is still deemed proper and is therefore made FINAL.

Claims 50-51 are newly added.

Claims 37-39 and 41-43 have been amended to read on the elected invention.

Claims 5, 11-25, 40, 44-49 are withdrawn from consideration for being drawn to a non-elected invention.

3. Claims 1-4, 6-10, 26-33, 37-39, 41-43, and 50-51 including SEQ ID NO:3, 11, 12, and 4 are examined in the present office action.

Specification

4. The Specification is objected to because the drawings are not referred to properly. If the drawings show Figures 1A-1E and Figures 2A-2B, then the Brief Description of the Drawings should recite "Figures 1A-1E and Figures 2A-2B", instead of "Figure 1" and "Figure 2". Correction is requested.

The specification is objected to on page 52, line 24, for not reciting the word "in" between the words "genes" and "transgenic".

Claim Objections

5. Claims 41-43 are objected to for being dependent on a non-elected base claim. Claims 41-43 will be examined to the extent that the limitations of the non-elected base claim are incorporated into claims 41-43. Correction is requested.

Claims 6-8 are objected to for being dependent on a non-elected base claim. Claims 6-8 will be examined to the extent that the limitations of the non-elected base claim is incorporated into claims 6-8. Correction is requested.

Claims 6-7, 9-10, 28, and 41-42 are objected to for being drawn to non-elected inventions, i.e., SEQ ID NO:1, 2, 9, and 10.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6-7, 9-10, 28-33, and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-7, 9-10, 28, 30, and 41-42 are indefinite because Applicants have not clearly defined what SEQ ID NO:3 and 4 represent. On page 19 of the specification, lines 13-15, Applicants disclose that SEQ ID NO:2 is the A. niger PhyA-2 polypeptide which has been produced by expression of the A. niger PhyA-2 gene of SEQ ID NO:1, which is the modified version of the naturally-occurring gene, i.e., more suitable for expression in plants. Applicants further disclose on page 19, lines 23-27, "To express the PhyA-1 polypeptide in plants, the present inventors modified the corresponding PhyA-1 gene sequence... and introduced a new translation start site immediately prior to and in-frame with, the nucleotide sequence encoding the mature PhyA-1 polypeptide". But then on page 48, lines 9-11, Applicants disclose that the modified PhyA-1 gene is set forth in SEQ ID NO:3 encoding SEQ ID NO:4. Claims drawn to SEQ ID NO:11 encoding SEQ ID NO:12 are included in the rejection because SEQ ID NO:11 comprises SEQ ID NO:3. Clarification is requested. New matter should be avoided.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 26-27, 30-33, 37-39, and 50-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a transgenic plant, progeny of the transgenic plant and a method of enhancing the phosphorus nutrition of a plant comprising transforming a plant with a nucleic acid molecule encoding a phytase, wherein the phytase is either any phyase (claims 1-3, 26-27, 30-33, 37-38, and 50-51), or wherein the phytase is from *Aspergillus niger* (claims 4 and 39).

Applicants disclose the isolation by PCR of a modified version of an *Aspergillus niger* PhyA-1 gene, designated as PhyA-2 (page 46, Example 1). As discussed above in the 112 2nd rejection, it is unclear exactly which SEQ ID NO corresponds with the native and modified PhyA gene. For both PhyA-1 and PhyA-2, Applicants disclose SEQ ID NO's corresponding to just the coding region and corresponding polypeptide and another pair of SEQ ID NO's corresponding to the coding region operably linked to a nucleic acid sequence encoding the carrot extensin secretion signal and corresponding polypeptide (page 19, lines 13-27; and page 22, lines 24-31).

The Applicants do not identify essential regions of the phytase protein encoded by SEQ ID NO:1 or 3, nor do Applicants describe any other polynucleotide sequences that encode a functional phytase protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise

definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a phytase protein falling within the scope of the claimed genus of polynucleotides. Applicants only describe a single cDNA sequence of SEQ ID NO:1 or 3. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the phytase protein, it remains unclear what features identify an *Aspergillus niger* phytase protein. Since the genus of phytase proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

8. Claims 1-4, 26-27, 30-33, 37-39, and 50-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a plant transformed with a nucleic acid sequence of SEQ ID NO:3 encoding SEQ ID NO:4 and wherein SEQ ID NO:3 is operably

linked to a nucleic acid encoding a signal peptide directing the secretion of said protein into the apoplast, and a plant transformed with SEQ ID NO:11 encoding SEQ ID NO:12, and method of enhancing the phosphorus nutrition in a plant and increasing the biomass of said plant; does not reasonably provide enablement for a transgenic plant comprising any nucleic acid molecule encoding any phytase or wherein said nucleic acid molecule encodes an *Aspergillus niger* phytase, or methods comprising said nucleic acid molecule, or wherein said transgenic plant or method comprises SEQ ID NO:3 encoding SEQ ID NO:4 or SEQ ID NO:11 encoding SEQ ID NO:12 and wherein said transgenic plant or method is for enhanced rate of epicotyl and hypocotyl production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a transformed plant or method of enhancing the phosphorus nutrition of a plant comprising, ectopically expressing in plant roots an isolated nucleic acid molecule encoding a phytase polypeptide and said phytase polypeptide is secreted from the roots,

or wherein secretion of the phytase is achieved by ectopically expressing the phytase as a fusion protein with a secretory signal peptide, or wherein the phytase is from *Aspergillus niger*; a progeny plant of the transformed plant ectopically expressing in its roots said isolated nucleic acid molecule and said phytase polypeptide is secreted from the roots, wherein said transformed plant or progeny plant exhibit an increased biomass, or enhanced rate of epicotyl or hypocotyl production. The claims are also drawn to a transformed plant or progeny plant comprising SEQ ID NO:11 encoding SEQ ID NO:12 wherein the plant or progeny plant exhibit an enhanced rate of epicotyl or hypocotyl production.

Applicants disclose amplifying the PhyA-1 gene from a plasmid that was obtained from Dr. Mullaney and making modifications to the PhyA-1 gene, i.e., deleting the leader sequence and the intron and introducing a new ATG translation start in the open reading frame, prior to the coding region for the mature protein (page 47 of the specification, bottom paragraph). The nucleotide sequence of the modified PhyA-1 gene is set forth in SEQ ID NO:3 encoding SEQ ID NO:4 (page 48, lines 9-11). Applicants operably linked a nucleic acid encoding the carrot extensin secretory signal sequence to SEQ ID NO:3 and the resulting sequence is set forth in SEQ ID NO:11 encoding SEQ ID NO:12 (page 48, line 13 to page 49, line 26). The resulting construct was transformed into Arabidopsis under the control of the CaMV 35S promoter (page 49, line 28, to page 51, line 17). Applicants disclose that plants transformed with said construct were able to utilize phytate as the sole source of phosphorus (page 59, line 29 to page 60, line 19).

The state-of-the-art teaches that not all phytases produce expected results. Wyss et al (1999, Applied and Environmental Microbiology 65(2):367-373) teach that the specific activities

of fungal phytases varies from 23 to 196 U per mg of protein and the pH optima ranged from 2.5 to 7.0. Wyss et al disclose that some phytases exhibited specific substrate specificity while others exhibited considerable activity with a broad range of phosphate compounds. In addition, some phytases exhibited a decreased activity as cleavage products accumulated (abstract).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences. In addition, Applicants have not taught how to measure enhanced epicotyl and hypocotyl production.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of any nucleic acid encoding any phytase as probes or by designing primers to undisclosed regions of any phytase and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed exhibit phytase activity and increase the available phosphorus to said plant. Furthermore, undue experimentation would be required to evaluate a multitude of exemplified or non-exemplified phytase genes for their ability to increase epicotyl and hypocotyl growth.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Deposit Rejection

9. Claims 8-9, 28, and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Since the plasmid claimed is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If a plasmid is not so obtainable or available, the requirements of 35 U.S.C. 112 may be satisfied by a deposit thereof. The specification does not disclose a repeatable process to obtain the exact same plasmid in each occurrence and it is not apparent if such a plasmid is readily available to the public. It is noted that applicants have specified plasmid AGAL Accession No. NM99/06795, but there is no indication in the specification as to public availability. If the deposit of plasmid is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the plasmid will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit, meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that

(a) during the pendency of the application, access to the invention will be afforded to the Commisioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) the viability of the biological material at the time of deposit will be tested (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, 4, 26-27, 30-33, 37, 39, and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Verwoerd et al (1995, Plant Physiol. 109:1199-1205), in light of Applicants' admitted statement of the prior art.

The claims are drawn to a transformed plant or method of enhancing the phosphorus nutrition of a plant comprising, growing said plant in a medium comprising phytate wherein the plant ectopically expresses in its roots an isolated nucleic acid molecule encoding a phytase polypeptide and said phytase polypeptide is secreted from the roots, or wherein secretion of the phytase is achieved by ectopically expressing the phytase as a fusion protein with a secretory signal peptide, or wherein the phytase is from *Aspergillus niger*; a progeny plant of the

transformed plant growing in a medium comprising phytate and wherein said plant ectopically expresses in its roots said isolated nucleic acid molecule and said phytase polypeptide is secreted from the roots, wherein said transformed plant or progeny plant exhibit an increased biomass, or enhanced rate of epicotyl or hypocotyl production, or wherein said phytase polypeptide is a fusion protein with a secretory signal peptide or wherein said phytate is a fertilizer phytate.

Verwoerd et al disclose a binary vector comprising a chimeric phytase gene encoding the tobacco PR-S signal peptide and a cDNA encoding the mature *Aspergillus niger* phytase gene, and tobacco plants transformed therewith (paragraph bridging pages 1199-1200, and page 1200, left column, bottom paragraph). Verwoerd et al disclose that the PR-S signal peptide functions in protein secretion in plants when attached to heterologous proteins. Verwoerd et al disclose that both primary transformants and progeny thereof, were grown in soil and comprised said chimeric phytase and that said phytase was found in extracellular fluid, showing that the enzyme was properly secreted to the intercellular space (page 1200, right column, top and bottom paragraphs; page 1201, left column, bottom paragraph; paragraph bridging pages 1201 and 1202; page 1202, 1st full paragraph). Given that Verwoerd et al utilize the constitutive CaMV 35S promoter, it would be inherent that the chimeric protein would be expressed and secreted in roots.

In addition, given that the transgenic plants of Verwoerd et al were grown in soil, they inherently are grown in a medium comprising phytate because Applicants disclose that soils contain phytate (see page 5, 2nd paragraph of specification; page 6, lines 4-5; page 8, lines 30-31; and page 9, lines 1-4), as discussed above. In addition, it would be inherent that the transformed

plants of Verwoerd et al exhibit an increased biomass or enhanced rate of epicotyl or hypocotyl production and as such, Verwoerd et al anticipate the claimed invention.

11. Claims 3, 6-10, 28-29, 41-43 and 50 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method of enhancing the phosphorus nutrition of a plant comprising transforming a plant with a nucleic acid comprising SEQ ID NO:3 encoding SEQ ID NO:4 or SEQ ID NO:11 encoding SEQ ID NO:12; or SEQ ID NO:3 operably linked to a nucleic acid molecule encoding a lupin acid phosphatase signal peptide or a carrot extensin signal peptide.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
December 8, 2004

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638